

**CLAIMS**

1. A process for producing an aldehyde derivative of a sialic acid in which a starting material having a sialic acid unit at the reducing terminal and a terminal saccharide at the non-reducing end which has a vicinal diol group is subjected to the sequential steps of:
- 5 a) preliminary selective oxidation to oxidise the vicinal diol group to an aldehyde
- b) reduction to reductively open the ring at the reducing terminal sialic acid unit, whereby a vicinal diol group is formed, and wherein the
- 10 aldehyde formed in step a) is also reduced to form a hydroxy group which is not part of a vicinal diol group; and
- c) selective oxidation to oxidise the vicinal diol group formed in step b) to form an aldehyde group.
2. A process according to claim 1 in which the sialic acid unit at
- 15 the reducing terminal is joined to the adjacent unit through the 8 carbon atom whereby in step b) the 6,7 vicinal diol group is oxidised to form an aldehyde on the carbon-7 atom.
3. A process according to claim 1 or claim 2 in which the saccharide unit at the non-reducing end is a sialic acid unit.
- 20 4. A process according to any preceding claim in which the starting material is a di-, oligo- or poly-saccharide.
5. A process according to claim 4 in which the polysaccharide is a polysialic acid consisting substantially only of units of sialic acid.
6. A process according to claim 5 in which the polysaccharide has
- 25 at least 2, preferably at least 5 or more preferably at least 10, most preferably at least 50 sialic acid units in the molecule.
7. A process according to any of claims 4 to 6 in which the preliminary oxidation step is carried out under conditions such that there is substantially no mid-chain cleavage of the polysaccharide chain.
- 30 8. A process according to claim 7 in which the preliminary oxidation step is carried out in aqueous solution in the presence of periodate

at a concentration in the range 1mM to 1M, a pH in the range 3 to 10, a temperature in the range 0 to 60°C and a time in the range 1 min to 48 hours.

9. A process according to any preceding claim in which step b) is carried out under conditions such that pendent carboxyl groups on the starting material are not reduced.

10. A process according to claim 9 in which step b) is carried out in aqueous solution in the presence of borohydride at a concentration in the range 1µM to 0.1M, a pH in the range 6.5 to 10, a temperature in the range 0 to 60°C and a period in the range 1 min to 48 h.

11. A process according to any preceding claim in which the aldehyde derivative is reacted with a substrate having a primary amine group or a hydrazide group.

12. A process according to claim 11 in which the product is reduced.

13. A process according to claim 11 or claim 12 in which the substrate is a peptide or a protein.

14. A process according to claim 13 in which the substrate is a peptide therapeutic.

15. A process according to claim 11 or claim 12 in which the substrate is a compound having a functional group substituent and a dibasic organic group joining the amine or hydrazide group and the functional group.

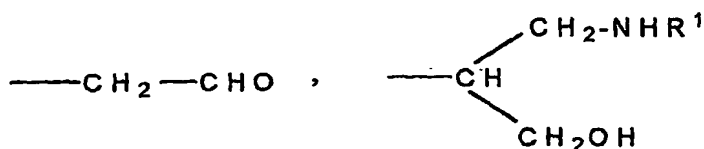
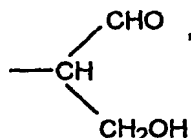
16. A process according to claim 15 in which the product is subsequently reacted with a compound having a thiol group, preferably a protein.

17. A process according to claim 11 or 12 in which the substrate is a drug delivery system, a cell, preferably a microbial cell or an animal cell, a virus or a synthetic polymer.

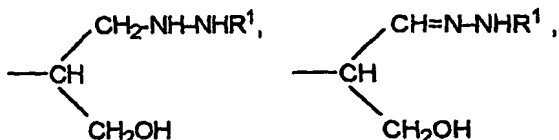
18. A compound which is an aldehyde derivative of a di-, oligo or poly-saccharide comprising at least one sialic acid unit, in which the terminal unit at the reducing end includes an aldehyde moiety or is a group OR, in

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which R is selected from



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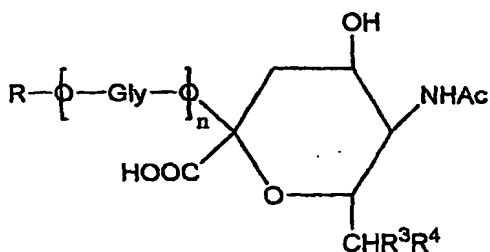


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$\text{---CH}_2\text{CH}_2\text{NHR}^1$ ,  $\text{CH}_2\text{CH=N---NHR}^1$  and  $\text{CH}_2\text{CH}_2\text{NHNHR}^1$  in which  $\text{R}^1$  is H,  $\text{C}_{1-24}$  alkyl, aryl  $\text{C}_{2-6}$  alkanoyl, or a polypeptide or a protein linked through the N terminal or the  $\gamma$ -amine group of a lysine residue, a drug delivery system or is an organic group having a functional substituent adapted for reaction with a sulfhydryl group and which has a passivated unit at the non-reducing end.

19. A compound according to claim 18 which has general formula I

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I

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in which  $\text{R}^3$  is H and  $\text{R}^4$  is OH.

20. A compound according to claim 18 or claim 19 which is a polysaccharide in which substantially all the saccharide units are of sialic acid, joined 2-8, 2-9 or alternating 2-8/2-9, to one another.

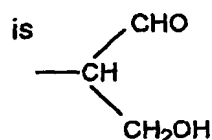
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21. A compound according to claim 20 having at least 2, preferably

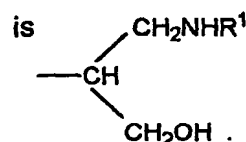
at least 5, more preferably at least 10, most preferably at least 50, sialic acid units in the polysaccharide chain.

22. A compound according to any of claims 18 to 21 in which R<sup>1</sup> is a protein or peptide or a drug delivery system.

5 23. A compound according to any of claims 18 to 22 in which R

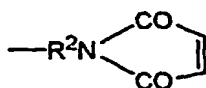


24. A compound according to any of claims 18 to 22 in which R



25. A compound according to claim 21 or claim 24 in which R<sup>1</sup> is a peptide or protein therapeutic, preferably an antibody or fragment.

26. A compound according to any of claims 18 to 21 in which R<sup>1</sup> is a group



in which R<sup>2</sup> is a dibasic organic group, preferably a

C<sub>2-12</sub>-alkanediyl group.

27. A composition comprising a compound according to any of claims 18 to 26 and a diluent.

28. A pharmaceutical composition comprising a compound according to claim 21 or claim 25 and a pharmaceutically acceptable excipient.